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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/868,884	02/05/2002	Andrew Baxter	06275-233001	7953

7590 01/13/2005

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EXAMINER	
TRUONG, TAMTHOM NGO	
ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/868,884	BAXTER ET AL.	
	Examiner	Art Unit	
	Tamthom N. Truong	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10-7-04 (RCE)*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,6-11 and 20-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *1-3,6-8,10,11,21-23,25 and 26* is/are allowed.

6)☒ Claim(s) *9,20 and 24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Pri rity under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10-07-04; 05-17-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after allowance or after an Office action under *Ex Parte Quayle*, 25 USPQ 74, 453 O.G. 213 (Comm'r Pat. 1935). Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, prosecution in this application has been reopened pursuant to 37 CFR 1.114. Applicant's submission filed on 10-07-2004 has been entered.

2. Claims 4, 5, and 12-19 are cancelled.

3. Claims 1-3, 6-11, and 20-26 are pending.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on 10-07-04 was filed with the RCE. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

The IDS of 5-17-04 is also considered herein.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 9, 20 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. Claim 9 recites a process with a step of "*converting the resultant compound of formula (I) into a further compound of formula (I)*", which is unclear as to which compound is converted into which.

b. Claim 20 recites a "*method of treating an IKK2 mediated disease...*" which has an indefinite metes and bounds because it is unclear what the intended diseases are.

c. Claim 24 recites "*multiple sclerosis*" lacks antecedent basis because "*multiple sclerosis*" is not an inflammatory disease as recited in claim 21.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. **Scope of Enablement:** Claims 20 and 24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of an inflammatory disease, does not reasonably provide enablement for the treatment of other IKK2 mediated disease or multiple sclerosis. The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

(1) The breadth of the claims;

(2) The amount of direction or guidance presented;

(3) The state of the prior art;

(4) The relative skill of those in the art;

(5) The predictability or unpredictability of the art;

(6) The quantity of experimentation necessary;

[See ***Ex parte Forman***, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also ***In re Wands***, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The breadth of the claims: Claim 20 recites a "method of treating an IKK2 mediated disease..." Said method covers the treatment of various diseases including: inflammatory diseases (e.g., rheumatoid arthritis, osteoarthritis, spondylitis, etc.), Reiters syndrome, psoriatic arthritis, lupus and bone resorptive disease, multiple sclerosis, inflammatory bowel disease, Crohn's disease, asthma, chronic obstructive pulmonary disease, emphysema, rhinitis, myasthenia gravis, Graves' disease, allograft rejection, psoriasis, dermatitis, allergic disorders, immune complex disease, cachexia, ARDS, toxic shock, heart failure, myocardial infarcts, atherosclerosis, reperfusion injury, AIDS, cancer, diabetes, dyslipidemia, obesity, polycystic

ovarian disease, hypertension, cardiovascular disease, and Syndrome X. Thus, the scope of claim 20 is very broad.

Claim 24 recites a "*method according to claim 21, wherein the disease is multiple sclerosis.*" Although the scope of claim 24 is narrow, "*multiple sclerosis*" is not an inflammatory disease. Moreover, the etiology of "*multiple sclerosis*" is currently unknown. Thus, the scope of claim 24 cannot be practiced.

The amount of direction or guidance presented: The specification only provides *in-vitro* assay for the inhibitory activity of the claimed compounds on IKK2. Since the inhibition of IKK2 associates with NIK, which in turn can inhibit NF-κB that treats inflammatory diseases, it would be reasonable to expect the claimed compounds to treat inflammatory diseases. However, there is no evidence if such an activity could treat heart failure, Graves' disease, AIDS, cancer, psoriasis, multiple sclerosis, etc. (or any other diseases that are allegedly associated with IKK2). Likewise, there is no evidence that the claimed compounds can reduce blood glucose level, or lipid, or cholesterol. Similarly, there is no evidence that the claimed compounds can inhibit mitosis for the treatment of cancer or cancer metastasis, nor is there evidence for the inhibition of HIV replication necessary for the treatment of AIDS. The specification simply does not provide sufficient guidance for the treatment of many diseases that are presumably associated with IKK2.

The state of the prior art: Currently, in the pharmaceutical art, no single compound can treat inflammatory disease, multiple sclerosis, heart failure, diabetes, asthma, cancer, AIDS, etc. for each of those diseases manifests itself differently, and affects different organs or systems. For example, drugs that treat arthritis such as NSAID's cannot be used to treat other diseases

including asthma which is an inflammatory condition. Likewise, drugs that treat cancer cannot treat AIDS since such an agent would suppress the immune system which would not be a benefit to an AIDS patient. Therefore, the state of the art does not provide guidance for the skilled clinician to treat IKK2 mediated diseases that are not an inflammatory disease.

The relative skill of those in the art: Even with the advanced training, the skilled clinician would have to establish a pharmacokinetics profile and a therapeutic index for each of the claimed compounds. Furthermore, one would have to weigh the ratio of 'risk to benefit' to treat each disease related to IKK2. Such a task would require extensive research which demands time, effort and resource.

The predictability or unpredictability of the art & The quantity of experimentation necessary: The pharmaceutical art is known for its unpredictability because the *in-vitro* activity does not always warrant the same *in-vivo* activity. Therefore, a mere showing of the *in*-vitro inhibition of IKK2 does not sufficiently guide the skilled clinician to treat various diseases that are presumably related to IKK2. Furthermore, treating various diseases using a single class of compounds does not conform to the standard practice of medicine. Thus, it would require undue experimentation for the skilled clinician to treat multiple sclerosis and other IKK2 related diseases.

Allowable Subject Matter

7. Claims 1-3, 6-8, 10, 11, 21-23, 25 and 26 are allowed.

8. The following is an examiner's statement of reasons for allowance:

Claims 1-3 and 6-8 are drawn to compounds of substituted 3-urea-2-thiophenecarboxamide. The closest prior art, **Gant et. al.** (WO 00/71532 A1), teaches compounds of substituted 2-urea-thiophene-3-carboxamide. However, said reference fails to teach a *phenyl* group as a substituent corresponding to the instant variable R^1. Thus, said reference does not anticipate or render obvious the instant compound claims as well as claims of pharmaceutical composition and method of treating inflammatory diseases.

The copending application 10/484,569 has claims reciting a proviso in the definition of "Z" which excludes thiophene compounds substituted with *phenyl-*$(CH_2)_nR^{11}$ or *phenyl-*$O(CH_2)_nR^{11}$ as claimed herein. Therefore, there is no issue of obviousness-type double patenting.

The copending application 10/484,645 has claims reciting thiophene compounds substituted with a *fused bicyclic ring system*, which cannot render obvious the instant compound claims, and claims of pharmaceutical composition as well as method of treating inflammatory diseases. Thus, there is no issue of obviousness-type double patenting either.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M-F (10:00-6:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Tamthom N. Truong
Examiner
Art Unit 1624

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01-06-05

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